Remarks

The above Amendments and these Remarks are in reply to the Office Action mailed April 6, 2005. A Petition for Extension of Time to Respond is submitted herewith, together with the appropriate fee.

The claims stand rejected under 35 U.S.C. §112, second paragraph as indefinite and under 35 U.S.C. §102(b) as anticipated by Sara (Biochim. Biophys. Res. Commun. 165:766-771 (1989), herein after "Sara."

Applicants have amended the claims to be drawn to methods for decreasing gonadotropin releasing hormone (GnRH) by the tripeptide, (1-3) IGF-1, otherwise known as glycyl-prolyl-glutamate, Gly-Pro-Glu, or GPE. Applicants respectfully submit that the claims are drafted in compliance with 35 U.S.C. §112, second paragraph, and are therefore, not indefinite. Further, Applicants submit that the identity of (1-3) IGF-1 and GPE is subject to official notice. However, if the Examiner believes that support for the equivalence of (1-3) IGF-1 and GPE is needed, the Applicants would be pleased to provide that evidence. Applicants submit that this subject matter is well described in the specification as filed, and working examples with data shown at least in Figures 2, 3, 7 and 8.

Regarding the rejections over Sara, Applicants note that Sara described her studies with GPE to include evidence that GPE potentiates potassium evoked release of (1) acteylcholine and (2) increased dopamine. Further, according to Sara, "[a]dditionally, GPE displays **agonist activity** at the NMDA receptor." Sara, page 770, second paragraph, lines 3-4; emphasis added. However, Sara neither discloses nor suggests any effect of GPE on release of GnRH or any other pituitary hormone.

In contrast with Sara, the instant application discloses an **antagonistic effect** of GPE on GnRH secretion induced by veratridine, a well known agent that acts by increasing calcium influx into cells.

Finally, Applicants would like to note that displacement of one ligand (e.g. ^{3}H glutamate) on a receptor (e.g., NMDA receptor) by an agent does not define the nature of the agent's effect on that receptor. That is, the agent could be (1) an agonist, (2) a partial agonist or (3) an antagonist. It is well known that determining whether an agent is either an agonist, partial agonist, or an antagonist depends upon measurement of an end-effect, for example, release of GnRH from the hypothalamus. Thus, the data of Sara relating to displacement of ^{3}H glutamate by GPE does not define the agonist or antagonist activity. In Sara, however, the effects of GPE to increase potassium-evoked release of acetylcholine or dopamine is consistent with an agonist effect of GPE on those neurotransmitters.

In contrast, Applicants have found that GPE is an antagonist, by virtue of the observed inhibition of veratridine-induced GnHR release. Thus, Applicant's observed effect is **opposite** to that described in Sara,

and therefore, Sara cannot anticipate Applicants' claims.

Enclosed is a PETITION FOR EXTENSION OF TIME UNDER 37 C.F.R. § 1.136 for extending the time to respond up to and including today, October 4, 2005.

If the Examiner believes that a telephone conversation with the undersigned would move the case forward, such a conversation is hereby invited.

The Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit Account No. 06-1325 for any matter in connection with this response, including any fee for extension of time, which may be required.

Respectfully submitted,

Date: October 4, 2005

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